

CLAIMS

What is claimed is:

1. A method of treating, preventing or managing macular degeneration, which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.
2. The method of claim 1, which further comprises administering to the patient a therapeutically or prophylactically effective amount of a second active agent.
3. The method of claim 2, wherein the second active agent is a steroid, a light sensitizer, an integrin, an antioxidant, an interferon, a xanthine derivative, a growth hormone, a neutrotrophic factor, a regulator of neovascularization, an anti-VEGF antibody, a prostaglandin, an antibiotic, a phytoestrogen, an anti-inflammatory compound or an antiangiogenesis compound.
4. The method of claim 2, wherein the second active agent is thalidomide, verteporfin, purlytin, an angiostatic steroid, rhuFab, interferon-2 α or pentoxifylline, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.
5. The method of claim 4, wherein the antiangiogenesis compound is thalidomide.
6. The method of claim 1, wherein the macular degeneration is wet macular degeneration, dry macular degeneration, age-related macular degeneration, age-related maculopathy, choroidal neovascularisation, retinal pigment epithelium detachment, atrophy of retinal pigment epithelium, Best's disease, vitelliform, Stargardt's disease, juvenile macular dystrophy, fundus flavimaculatus, Behr's disease, Sorsby's disease, Doyne's disease, honeycomb dystrophy, or macular damaging condition.
7. The method of claim 1, wherein the selective cytokine inhibitory drug is stereomerically pure.
8. A method of treating, preventing or managing macular degeneration, which comprises administering to a patient in need of such treatment, prevention or management a

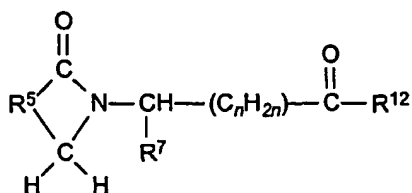
therapeutically or prophylactically effective amount of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

9. The method of claim 8, wherein the 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide is enantiomerically pure.

10. A method of treating, preventing or managing macular degeneration, which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount of cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

11. The method of claim 10, wherein the cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide is enantiomerically pure.

12. The method of claim 1, wherein the selective cytokine inhibitory drug is of formula (I):



(I)

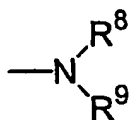
wherein *n* has a value of 1, 2, or 3;

R^5 is *o*-phenylene, unsubstituted or substituted with 1 to 4 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkyl of 1 to 10 carbon atoms, and halo;

R^7 is (i) phenyl or phenyl substituted with one or more substituents each selected independently of the other from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (ii) benzyl

unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (iii) naphthyl, and (iv) benzyloxy;

- 5 R^{12} is -OH, alkoxy of 1 to 12 carbon atoms, or

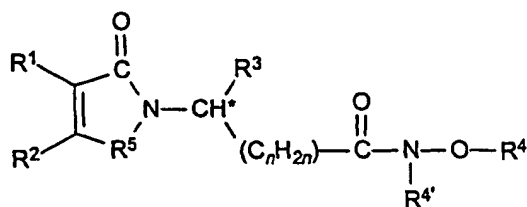


R^8 is hydrogen or alkyl of 1 to 10 carbon atoms; and

R^9 is hydrogen, alkyl of 1 to 10 carbon atoms, $-COR^{10}$, or $-SO_2R^{10}$, wherein R^{10} is hydrogen, alkyl of 1 to 10 carbon atoms, or phenyl.

- 10 13. The method of claim 12, wherein the selective cytokine inhibitory drug is enantiomerically pure.

14. The method of claim 1, wherein the selective cytokine inhibitory drug is of formula (II):



- 15 (II)

wherein each of R^1 and R^2 , when taken independently of each other, is hydrogen, lower alkyl, or R^1 and R^2 , when taken together with the depicted carbon atoms to which each is bound, is *o*-phenylene, *o*-naphthylene, or cyclohexene-1,2-diyl, unsubstituted or substituted with 1 to 4 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo;

R^3 is phenyl substituted with from one to four substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, alkylthio of 1 to 10 carbon atoms, benzyloxy, cycloalkoxy of 3 to 6

carbon atoms, C₄-C₆-cycloalkyldenemethyl, C₃-C₁₀-alkyldenemethyl, indanyloxy, and halo;

R⁴ is hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, or benzyl;

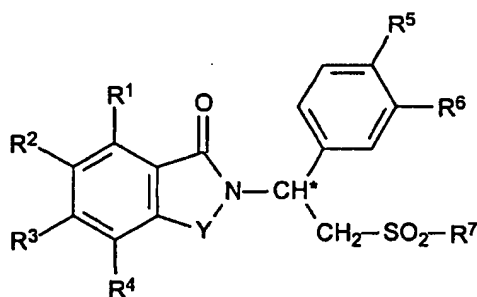
R^{4'} is hydrogen or alkyl of 1 to 6 carbon atoms;

5 R⁵ is -CH₂-, -CH₂-CO-, -SO₂-, -S-, or -NHCO-; and

n has a value of 0, 1, or 2.

15. The method of claim 14, wherein the selective cytokine inhibitory drug is enantiomerically pure.

10 16. The method of claim 1, wherein the selective cytokine inhibitory drug is of formula (III):



(III)

wherein the carbon atom designated * constitutes a center of chirality; Y is C=O, CH₂, SO₂, or CH₂C=O;

15 each of R¹, R², R³, and R⁴, independently of the others, is hydrogen, halo, alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, nitro, cyano, hydroxy, or -NR⁸R⁹; or any two of R¹, R², R³, and R⁴ on adjacent carbon atoms, together with the depicted phenylene ring are naphthylidene;

20 each of R⁵ and R⁶, independently of the other, is hydrogen, alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, or cycloalkoxy of up to 18 carbon atoms;

R⁷ is hydroxy, alkyl of 1 to 8 carbon atoms, phenyl, benzyl, or NR⁸R⁹;

25 each of R⁸ and R⁹ taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of R⁸ and R⁹ is hydrogen and the other is -COR¹⁰ or -SO₂R¹⁰, or R⁸ and R⁹ taken together are tetramethylene, pentamethylene, hexamethylene, or -CH₂CH₂X¹CH₂CH₂- in which X¹ is -O-, -S- or -NH-; and

each of $R^{8'}$ and $R^{9'}$ taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of $R^{8'}$ and $R^{9'}$ is hydrogen and the other is $-COR^{10'}$ or $-SO_2R^{10'}$, or $R^{8'}$ and $R^{9'}$ taken together are tetramethylene, pentamethylene, hexamethylene, or $-CH_2CH_2X^2CH_2CH_2-$ in which X^2 is $-O-$, $-S-$, or $-NH-$.

5 17. The method of claim 16, wherein the selective cytokine inhibitory drug is enantiomerically pure.

10 18. A method of treating, preventing or managing macular degeneration, which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, before, during or after surgical intervention directed at reducing or avoiding a symptom of macular degeneration in the patient.

15 19. The method of claim 17, wherein the surgical intervention is light therapy, laser therapy, radiation therapy, retinal pigment epithelium transplantation, or foveal translocation.

20 20. A pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, and a second active agent capable of reducing or avoiding a symptom of macular degeneration.

20 21. The pharmaceutical composition of claim 20, wherein the second active agent is a steroid, a light sensitizer, an integrin, an antioxidant, an interferon, a xanthine derivative, a growth hormone, a neutrotrophic factor, a regulator of neovascularization, an anti-VEGF antibody, a prostaglandin, an antibiotic, a phytoestrogen, an anti-inflammatory compound or an antiangiogenesis compound.

25 22. The pharmaceutical composition of claim 20, wherein the second active agent is thalidomide, verteporfin, purlytin, an angiostatic steroid, rhuFab, interferon- 2α or pentoxifylline, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.